

# Neonatal Pain: Theory and Concepts

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## Abstract

Pain assessment and management in the neonatal population is an on-going area of controversy and debate. Historically a lack of knowledge and understanding of neonatal pain has hindered the development of comprehensive pain management strategies in the clinical area. The rights of the child to appropriate pain relief regardless of the environment is paramount, however most pain interventions are of uncertain efficacy and are associated with both risk and cost.

This paper examines current literature on the theory and concepts associated with neonatal pain. The first section will review evidence on the deleterious effect of pain on the neonate. The second section considers to what extent existing evidence had influenced neonatal pain assessment, reviewing the strategies utilised to assess pain within this specialised population.

## Introduction

Debate on the management of neonatal pain has evolved over the past three decades. The initial widespread belief that neonates lack complete development of the neuroanatomical and neuroendocrine components necessary to perceive pain, accompanied by concerns over the potentially deleterious effects of analgesia on the respiratory system (Lippmann et al. 1976, Rackow et al. 1961) informed clinical practice at that time, with neonates receiving inadequate or no analgesia for painful procedures.

Anera of research in the 1980's established that neonates did demonstrate similar or exaggerated physiological and hormonal responses to pain (Anand and Hickey 1987), highlighting that exposure to pain may increase neonatal morbidity (Anand et al. 1987).

It is now acknowledged that neonates experience pain to a similar extent or possibly more intensely than older children and adults and are at risk of adverse long term behavioural and developmental effects due to inadequate management of pain relief in the newborn period (Mathew and Mathew 2003). However regardless of these

views it is still reported that pain is:

*"..underestimated and under treated in children and particularly babies. There is still evidence that pain is inadequately dealt with for children, requiring better prevention, assessment and treatment".*

(Department of Health, Department for Education and Skills 2007)

Furthermore the intense debate over the dosage of analgesia as well as the risks and benefits of different pain management techniques within the neonatal population continue within the literature (Anand et al. 2004).

## Effects of Pain on the Neonate

The short and long-term effect of pain on the term and preterm neonate is a complex area of discussion. The increasing number of surviving extremely low birth weight and medically fragile neonates has introduced a new population into the Neonatal Intensive Care Unit (NICU) who potentially can be hospitalised for lengthy periods (Grunau and Tu 2007). It has also been suggested that due to the plasticity of the developing nervous system, the greatest impact of pain may occur in the most immature and sick neonate (Fitzgerald 2005).

Within the NICU environment neonates are frequently exposed to repeated stressful and nociceptive stimulation

which can lead to sensitization (Grunau and Tu 2007), with excessive or abnormal neural activity related to pain and injury during the postnatal period also being linked to long-term changes in somatosensory and pain processing (Anand 2000). Procedural pain can induce changes in physiological, behavioural and hormonal response which could influence nociceptive and tactile thresholds, neurodevelopment, stress physiology and behaviour (Anand 2000).

There is also a growing body of evidence which suggests a potential link between pain in preterm neonates (particularly extreme preterm) to later development and behavioural compromise in preterm children (Grunau and Tu 2007). Furthermore Anderson et al. (2004) highlight a correlation between problems in cognitive and behavioural function and birth weight and gestational age. It has also been suggested that the intensity of pain experienced by the neonate in the NICU is another important factor in neurodevelopmental outcome (Grunau and Tu 2007).

## Differentiation between Pain and Stress in the Neonate

The terms "neonatal pain" and "neonatal stress" frequently interlink in the literature. The fact that the neonate cannot report pain presents challenges in the assessment and management of both stress and pain in the neonatal period (Johnston et al. 1997). Stress has been defined as:

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Keywords  
Neonatal Pain, Pain Assessment,  
Pain Scales, Pain Indicators.

*“a physical, chemical, or emotional factor that cause’s bodily or mental tension and may be a factor in disease causation”* (Merriam Webster 1994 p1164).

Stress responses can be specific to a particular source or nonspecific and generalised. McIntosh et al. (1993) reflected that pain is always stressful however stress is not necessarily painful. It is however extremely difficult in a nonverbal neonate to distinguish where stress ends and the painful experience begins.

Grunau and Tu (2007 p 45) reflect that: *“Conceptually, pain is on a continuum of stressors from handling to skin-breaking procedures”*.

Stokowski (2009) in a review which discussed the quantification of neonatal stress highlighted that there was a great deal of overlap in what was considered to be painful and what was considered to be stressful to the neonate. The author goes on to reflect that there is currently no validated tool to measure neonatal stress levels. This view was supported by Grunau and Tu (2007 p45), reflecting that with reference to the multiple aspects of bio behavioural reactivity in the neuro-physiologically immature neonate, the separation of specific sensory changes which occur as a result of pain, are very difficult to differentiate from the cumulative effects of pain and stress.

The American Academy of Pediatrics (AAP) also acknowledge that behaviours associated with pain may also be associated with perceived non painful care-giving procedures, going on to recommend additional research to better differentiate pain and stress be conducted (American Academy of Pediatrics 2000).

### The Assessment of Neonatal Pain: Theory to Practice

The plethora of literature on neonatal pain has undoubtedly had the potential to influence practice, however the extent to which this is reflected in the clinical area is inconsistent. The need to prevent pain whenever possible or have strategies in place to ensure effective pain management is acknowledge as a priority (RCN 2009). Nevertheless despite guidelines for neonatal pain management being aimed at addressing these issues (American Academy of Pediatrics 2000, 2006, Association of Paediatric Anaesthetists of Great Britain and Northern

Ireland 2012), non-adherence to guidelines in the clinical area continues to be reported (Hansen and Severinsson 2009, Lugtenberg et al. 2009).

However it has to be acknowledged that neonatal pain assessment is a complex and challenging issue, with multiple factors potentially affecting neonatal pain response and therefore influencing appropriate assessment strategies. This may include the gestational age of the neonate (Grunau and Tu 2007), severity of illness (Stevens et al. 1994), level of sedation (Ramsay 2000) and specific pathology such as neurological impairment (Stevens et al. 2007b). Also highlighted are the different situations and environments within which the neonate may experience pain and the lack of specificity to this influencing factor in pain indicators (Stevens et al. 2007b). Due to variables within the neonatal population, methods of pain assessment may not be fully generalizable to different age groups such as the preterm and term baby. Therefore a degree of caution should be applied when reviewing various methods of pain assessment with particular reference to their validation sample (Stevens et al. 2007b).

### Physiological Measures of Assessing Neonatal Pain

There is an increasing body of literature which examines the utilisation of physiological measures as an indicator of pain in the neonate (Sweet and McGrath 1998, Stevens et al. 1995, Raeside 2011). Physiological measures of pain adopt the assumption that changes in physiological variables are indicative of pain (Hester 1993), these measures may include changes in heart rate, vagal tone, respiratory rate, blood pressure, palmer sweating, oxygen saturation, transcutaneous oxygen tension, transcutaneous carbon dioxide tension, and intracranial pressure. However it has been suggested that the validity and reliability of these physiological measures are questionable due to the subjective and labile nature of pain itself (McGrath 1996). Regardless of these concerns, physiological measures are proposed as being quantifiable and objective in nature, despite the difficulties in establishing their validity, reliability, specificity, sensitivity and practicality (Stevens et al. 1995).

Sweet and McGrath (1998) suggest

that despite the difficulties in assessing psychometric properties of physiological pain indicators, there may be other characteristics which can be examined to support the reliability, validity and specificity of physiological measures of pain. This includes demonstrating that there is a change in the physiological indicator of pain when analgesics are used as opposed to when they are not, and also differences in physiological indicators when painful and non-painful procedures are compared. The practicality of utilising physiological parameters in various clinical settings should also be considered, with some pain assessment measures being useful in a research setting but not a clinical setting.

A novel approach, Near-infrared spectroscopy (NIRS), measures neonatal pain responses at a cortical level and offers opportunities to assess pain and validate neonatal pain assessment tools (Holsti et al. 2011). NIRS works by evaluating acute changes in cerebral blood flow, volume and oxygenation which provides indices of activity in the somatosensory cortex which have been used to evaluate cortical responses to pain for many years (Edwards et al. 1988). However despite this brain-based method providing an innovative way of understanding pain, the issue of whether cortical activation is a direct indicator of pain is unclear. When used as a clinical bedside tool NIRS can be challenging as results can be affected by movement artefacts (Wolf and Griesen 2009). However the use of NIRS does provide scope for development in future pain research studies (Holsti et al. 2011).

### Behaviour Indicators in the Measure of Neonatal Pain

Behaviour has been viewed as being a useful measure and indicator of neonatal pain (McGrath 1996). There are several reasons why behaviour should be considered, it is often the first sign of pain and may set the template for the developing child’s reaction to painful events and later coping strategies (McGrath 1996). Interestingly it has been suggested in early research that a crying child was an important determinant in how nurses’ rated pain and the level of intervention initiated, researchers observed that a child that did not cry or vocalise pain was less likely to be given analgesics (Hamers et al. 1994). Behaviour as a reaction to pain can be divided into

different phases. The initial phase is the immediate reaction to noxious stimuli, characterised by a range of behaviours such as withdrawal, grimacing, flailing or crying, with this immediate reaction being followed by a more subtle reaction to on-going pain in a shutdown of activity or “non-responsive” phase (McGrath 1998).

However as pain is subjective, behavioural assessment is indirect and therefore it can be argued that it is never entirely accurate (Merskey and Bogduk 1994). Furthermore many behavioural measures lack clinical validation and therefore may be problematic in the research setting, according to Barr (1998) there is dissociation between physiological and behavioural responses. However psychometric testing of behavioural tools is an on-going area of development in order to obtain reliability and validity for these measures. Several studies have examined the different behavioural responses of both preterm (Stevens et al. 1994, Craig et al. 1993, Grunau et al. 2004) and term babies (Gibbons et al. 2002, Stevens et al. 2004) to painful events such as heel lance or circumcision.

Facial expression is viewed as being a reliable and consistent behavioural indicator of pain which can apply across situations and populations (Stevens et al. 2007a). Cry has also been reported extensively throughout the years in assessment of neonatal pain (Wasz-Hockert et al. 1987). It is most frequently described in terms of presence or absence (Owens and Todt 1984), amplitude, pitch and temporal characteristics. In the NICU and the transport setting cry may be of limited value as babies are frequently ventilated and cannot cry or vocalise. Body movements have also been reported as pain indicators in the neonatal period, however gestational age has an important influence on the type and frequency of the body movement, with the preterm or acutely ill infant lacking the energy reserves to display movement. The extremely preterm infant exposed to frequent painful procedures may become limp and flaccid in response to pain, with their movements being more disorganised than the healthy term neonate (Stevens et al. 2007b).

### Biomarkers as an Indicator of Pain

The identification of a readily available marker of pain which is not subjective or

ambiguous would greatly enhance the assessment and management of pain (Stevens et al. 2007b). The pain system offers several potential biomarkers within its related endocrine, neural substrate, immune and genetic components. Biomarkers may include leukocyte count (WBC), temperature or C-reactive protein (CRP) as indices of infection or inflammation and the subsequent response to treatment, with cortisol, endorphins and growth hormone also being studied as indices of pain (Anand and Hickey 1992). Salivary cortisol has also been widely used as a biomarker of stress/pain responses of the hypothalamic-pituitary-adrenal system (Walker et al. 2001). Cortisol is the primary human hormone, however there are conflicting data on cortisol secretion in the neonatal period with reports that cortisol levels are higher in sick rather than healthy preterm neonates (Economou et al. 1993).

Scott and Wattenberg (1995) support this view reporting that plasma cortisol levels correlate with gestational age and severity of illness. Stevens et al. (2007b) however highlight that no single biomarker characterises all aspects of neonatal pain, with the pain system having complex interrelationships with other reactivity systems.

### Strategies in Pain Assessment

Having considered the effects of pain on the neonate and the measurement of pain, it is crucial to then consider how to achieve appropriate pain assessment in the clinical setting. Several areas have to be considered when a measure of pain assessment is introduced into clinical practice. Assurance that the measure assesses pain in a reproducible way will be dependent on psychometric properties (Streiner and Norman 2006). However it is important to acknowledge that modifications to a pain measure in an attempt to adapt to different environments or client groups may interfere with psychometric testing and therefore will require new testing.

Pain measurement can be classified as behavioural, physiological or self-report, however due to the neonates’ inability to self-report this method cannot be applied. Neonatal pain assessment measures can be further classified as unidimensional or multidimensional with composite measures. Multidimensional

strategies utilise more than one type of pain indicator with composite measures also incorporating contextual strategies such as sleep state (Stevens et al 2007b).

### Multidimensional Pain Measures

Due to the complexities in pain assessment many adopt the view that multidimensional pain measures are the most appropriate (Duhn and Medves 2004). Furthermore it has been reported that correlation between physiological and behavioural indicators is consistently low in unidimensional measurement strategies (Stevens et al. 2007b). However both subjective and objective data are adopted in a multidimensional approach, this can be done by assessing different elements in a particular domain such as facial actions, cry and body movement. Alternatively a composite measure can be used that include multiple domains such as physiological, behavioural and contextual indicators. There has been a rapid increase in the number of multidimensional pain assessment scales available for application within the clinical setting over recent years (Duhn and Medves 2004).

### Unidimensional Pain Measures

A unidimensional measure will utilise one indicator to assess pain such as infant heart rate, or use several indicators from one domain such as heart rate, blood pressure and breathing rate. Behavioural indicators of infant pain have however traditionally been the most widely utilised, this would include cry, facial expression and activity.

However when assessing behavioural indicators non-verbal infants present the challenge of distinguishing between pain and other states such as hunger or agitation. Despite confounding factors influencing behavioural indicators such as severity of illness, neurological influence, pharmacological influence and extreme prematurity, behavioural indicators within pain assessment scales continue to be reported as one of the most reliable indicators of infant pain (Hudson-Barr et al. 1998).

### Reliability and Validity of Pain Assessment Scales

Reliability and validity testing is an important element in the introduction of a pain assessment scale to the clinical area (Duhn and Medves 2004). However despite the extensive number

of available scales, all of the assessment related problems in neonates have not been solved. Duhn and Medves (2004) highlight that most scales have been validated for the acute, procedural setting and perform less well for sub-acute or chronic pain.

Thewissen and Allegaert (2011) argue that most scales do not take into account persistent pain which results in a quiet immobile neonate and also the limited capacity of the preterm neonate to mount a consistent and persistent behavioural and physiological response to pain. However newly evolving scales such as the N-PASS pain and sedation scale (Hummel et al. 2008) is an example of a scale which encompasses both pain and sedation with inclusion of the inactive and preterm neonate.

The validation and implementation of a pain scale may be based on intra and inter individual variability, with correlations being made with neuroendocrine markers of pain and stress (Fitzgerald and Walker 2009). However it has been highlighted by Thewissen and Allegaert (2011) that interrater agreement is only reflective of agreement in rating between different caregivers and excludes a systematic error. It has been suggested that pain assessment scales focus on aspects of pain expression which does not necessarily reflect nociception (Fitzgerald and Walker 2009).

A further aspect presented by Xavier Balda et al. (2000) is that health professionals under assess infant pain as a coping strategy, reflecting that this occurs during times when health professionals are put in a position when they need to cause varying degrees of pain and discomfort to the neonate as part of their daily job. Reyes (2003) expand on this view by highlighting the importance of nurses' appropriate assessment and subsequent documentation of pain. Frequently pain assessment scales are modified and adapted to particular clinical areas where they will be used, however modification of pain assessment scales or application in a new population or environment may interfere with psychometric testing and may necessitate repeat testing (Duhn and Medves 2004). The issue of clinical utility is important as it has to be appropriate for use in the clinical setting. Scales which are complex, lengthy and require extensive training may not be feasible or practical in the clinical setting. It is important to

ascertain if the scale or measure has been developed for research or clinical purposes and the population within which the scale has been developed (Streiner and Norman 2006).

### Conclusion

This Paper provides an overview of the complex issues surrounding neonatal pain and the extreme difficulties in assessing pain in this group of patients. The treatment of pain in neonates stimulates debate around ethical issues, health policy frameworks and clinical practice. The rights of the neonate to appropriate pain relief regardless of the circumstances or environment is paramount. However some pain interventions within this population are of uncertain efficacy, fuelling controversy in relation to assessing risk and benefit.

Despite a plethora of literature on the detrimental effects of neonatal pain accompanied by clear agreement that neonates experience pain, there continues to be reports of inadequate assessment of pain in the clinical area and underuse of pain assessment strategies. The reasons speculated for this range from difficulties in the application of some pain scales to the clinical area, challenges in differentiating pain and stress, to lack of education or training. This provides challenges for future research and clinical practice to develop safe and effective strategies in pain management within this vulnerable population, accompanied by effective education programmes.

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